UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,668	02/24/2004	Joseph F. Foss	P0453.70113US04	2689

7590 01/05/2006

Edward R. Gates
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
GRAFFEO, MICHEL	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 01/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/785,668	FOSS ET AL.	
	Examiner	Art Unit	
	Michel Graffeo	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-8 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/13/04; 8/9/04; 6/14/04; 2/24/04;
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Action

The preliminary Amendment (Filed 3 June 2004) amended claims 1-5 and 8. Claims 1-8 are pending and examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 2-3 the phrase in quotes "(or a dose of another opioid...)" is tantamount to the phrase "for example" which renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 4,176,186 to Goldberg et al.

Goldberg et al. teach a method for treating the intestinal mobility inhibiting (constipation) side effects (in current claims 1-7; see Abstract) of for example, methadone (in current claims 1-3; see col 7 line 38) with quaternary derivatives of noroxymorpone (in current claims 1-7; see Title) enterically or parenterally for example (in current claims 6-7; see col 7 lines 48-56) via coated pills, tablets solutions, suspensions etc wherein the dosage unit is from 0.133mg/kg to 1.33mg/kg.

Although Goldberg et al. do not specifically teach the plasma concentrations reached or time frame for treatment of the actives, such is necessarily the case since the dosage and administration is the same the plasma concentrations must be the same. Moreover, products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical compound, the properties applicant discloses and/or claims are necessarily present.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the

> subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yuan et al. Methylnaltrexone prevents morphine-induced delay in oral-cecal transit time without affecting analgesia: A double-blind randomized placebo-controlled trial. Clin. Pharmacol Ther. 1996;59:469-75 in view of US Patent No. 4,176,186 to Goldberg et al.

Yuan et al. teach a method of treating morphine induced constipation (induce laxation) with 0.45mg/kg methylnaltrexone administered intravenously and suggests that the methylnaltrexone can be administered as an adjunct to opioids for the relief of opioid induced constipation (in current claims 1-3, 5 and 8; see Abstract). Additionally, Yuan et al. show in Fig 1 that dosed individuals oral-cecal time started in some cases in less than 90 minutes (in current claims 1 and 4; see page 471).

Yuan et al. do not recite the particular dosage ranges as claimed.

Goldberg et al. teach a method for treating the intestinal mobility inhibiting (inducing laxation) side effects (in current claims 1-7; see Abstract) of for example, methadone (in current claims 1-3; see col 7 line 38) with quaternary derivatives of noroxymorpone (in current claims 1-7; see Title) enterically or parenterally for example (in current claims 6-7; see col 7 lines 48-56) via coated pills, tablets solutions, suspensions etc wherein the dosage unit is from 0.133mg/kg to 1.33mg/kg.

Although neither Yuan et al. nor Goldberg et al. teach that the plasma concentrations of the actives maintained below the claimed range, such is necessarily the case since the dosage and administration is the same, the plasma concentrations must be the same. Moreover, products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical compound, the properties applicant discloses and/or claims are necessarily present.

One of ordinary skill in the art would have been motivated to combine the above references and as combined would teach the invention as claimed. One of ordinary skill in the art would have been motivated to combine Yuan et al. and Goldberg et al. because both are directed to the treatment of constipation in a patient in need wherein the needs arises from another treatment, specifically wherein that other treatment comprises an opioid. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

Yuan et al. Effects of methylnaltrexone on chronic opioid-induced gut motility and transit time changes. Abstracts from the Eighth International Symposium on Pain, Anesthesia and Endocrinology. September 18-19, 1997 is considered an equivalent to US Patent No. 4,176,186 to Goldberg et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 are provisionally rejected on the ground of nonstatutory double patenting over claims 1-2, 13-16 and 19-22 of copending Application No. 10/778268 in view of US Patent No. 4,176,186 to Goldberg et al. and Yuan et al. Methylnaltrexone prevents morphine-induced delay in oral-cecal transit time without affecting analgesia: A double-blind randomized placebo-controlled trial. Clin. Pharmacol Ther. 1996;59:469-

75. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully claimed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: A method for treating constipation in a patient receiving opioids chronically, comprising administering to the patient receiving opioids chronically a quaternary derivative of noroxymorphone in an amount such that peak plasma concentrations of the quaternary derivative of noroxymorphone do not exceed 100 ng/ml.

Although the instant application does not recite a limitation of laxation within 24 hours, since the dosage amounts are the same, the compounds functionality must necessarily be the same. Also, in light of Yuan et al. which teaches that dosed individuals oral-cecal time started in some cases in less than 90 minutes, one of ordinary skill in the art would find the claims obviously claimed in the '268 application. The instant application does not claim parenterally administering the derivative, but nonetheless one of ordinary skill in the art would find the oral administration obvious in light of the teachings in Goldberg et al.

Claims 1-8 are provisionally rejected on the ground of nonstatutory double patenting over claims 1-2, 13-16 and 19-22 of copending Application No. 10/779128 in view of US Patent No. 4,176,186 to Goldberg et al. and Yuan et al. Methylnaltrexone

prevents morphine-induced delay in oral-cecal transit time without affecting analgesia: A double-blind randomized placebo-controlled trial. Clin. Pharmacol Ther. 1996;59:469-75. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully claimed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: A method for treating constipation in a patient receiving opioids chronically, comprising administering to the patient receiving opioids chronically a quaternary derivative of noroxymorphone in an amount such that peak plasma concentrations of the quaternary derivative of noroxymorphone do not exceed 100 ng/ml.

Although the instant application does not recite a limitation of laxation within 24 hours, since the dosage amounts are the same, the compounds functionality must necessarily be the same. Also, in light of Yuan et al. which teaches that dosed individuals oral-cecal time started in some cases in less than 90 minutes, one of ordinary skill in the art would find the claims obviously claimed in the '128 application. The instant application does not claim parenterally administering the derivative, but nonetheless one of ordinary skill in the art would find the oral administration obvious in light of the teachings in Goldberg et al.

Claims 1-8 are provisionally rejected on the ground of nonstatutory double patenting over claims 1-8 of copending Application No. 10/785320.

This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully claimed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: A method for treating constipation/inducing laxation in a patient receiving opioids chronically, comprising administering orally to the patient receiving opioids chronically a quaternary derivative of noroxymorphone in an amount to achieve laxation within 24 hours wherein said amount is such that peak plasma concentrations of the quaternary derivative of noroxymorphone do not exceed 100 ng/ml.

Claims 1-8 are provisionally rejected on the ground of nonstatutory double patenting over claims 1 and 18-33 of copending Application No. 10/278630 in view of US Patent No. 4,176,186 to Goldberg et al. and Yuan et al. Methylnaltrexone prevents morphine-induced delay in oral-cecal transit time without affecting analgesia: A double-blind randomized placebo-controlled trial. Clin. Pharmacol Ther. 1996;59:469-75 This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully claimed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: A method for preventing opioid induced inhibition of gastrointestinal motility comprising orally administering an enterically coated quaternary derivative of noroxymorphone to a patient prior to the administration of an opioid.

Although the instant application does not recite a limitation of laxation within 24 hours, since the dosage amounts are the same, the compounds functionality must necessarily be the same. Also, in light of Yuan et al. which teaches that dosed individuals oral-cecal time started in some cases in less than 90 minutes, one of ordinary skill in the art would find the claims obviously claimed in the '630 application.

Claims 1-8 are provisionally rejected on the ground of nonstatutory double patenting over claims 29-46 of copending Application No. 10/779129 in view of US Patent No. 4,176,186 to Goldberg et al. and Yuan et al. Methylnaltrexone prevents morphine-induced delay in oral-cecal transit time without affecting analgesia: A double-blind randomized placebo-controlled trial. Clin. Pharmacol Ther. 1996;59:469-75. This is a provisional double patenting rejection since the conflicting claims have not yet been patented. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully claimed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: A method for treating a patient with a gastrointestinal dysfunction caused by endogenous opioids, comprising administering to the patient an amount of a quaternary derivative of noroxymorphone effective to treat the gastrointestinal dysfunction.

Although the instant application does not recite a limitation of laxation within 24 hours, since the dosage amounts are the same, the compounds functionality must necessarily be the same. Also, in light of Yuan et al. which teaches that dosed individuals oral-cecal time started in some cases in less than 90 minutes, one of ordinary skill in the art would find the claims obviously claimed in the '268 application. Although the reference application does not specifically claim oral administration, one of ordinary skill in the art would have found such administration to be obvious over Goldberg et al.

Claims 1-8 rejected on the ground of nonstatutory double patenting over claims 1-38 of U. S. Patent No. 6,608,075 in view of Yuan et al. Methylnaltrexone prevents morphine-induced delay in oral-cecal transit time without affecting analgesia: A double-blind randomized placebo-controlled trial. Clin. Pharmacol Ther. 1996;59:469-75 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully claimed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: A method for preventing opioid induced inhibition of gastrointestinal motility comprising orally administering an enterically coated quaternary derivative of noroxymorphone to a patient prior to the administration of an opioid, wherein the patient's plasma level of the quaternary derivative of noroxymorphone does not exceed 50 ng/ml.

Although the instant application does not recite a limitation of laxation within 24 hours, since the dosage amounts are the same, the compounds functionality must necessarily be the same. Also, in light of Yuan et al. which teaches that dosed individuals oral-cecal time started in some cases in less than 90 minutes, one of ordinary skill in the art would find the claims obviously claimed in the '075 patent.

Claims 1-8 rejected on the ground of nonstatutory double patenting over claims 1-36 of U. S. Patent No. 6,559,158 in view of US Patent No. 4,176,186 to Goldberg et al. and Yuan et al. Methylnaltrexone prevents morphine-induced delay in oral-cecal transit time without affecting analgesia: A double-blind randomized placebo-controlled trial. Clin. Pharmacol Ther. 1996;59:469-75 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully claimed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: A method of preventing or treating an opioid-induced side

effect in a chronic opioid patient, the method comprising administering a quaternary derivative of noroxymorphone in an amount sufficient to prevent or treat the side effect in the patient, wherein said amount is insufficient to treat the side effect in a patient to whom opioids have not been chronically administered and wherein said amount is such that peak plasma concentrations do not exceed 100 ng/ml.

Although the instant application does not recite a limitation of laxation within 24 hours, since the dosage amounts are the same, the compounds functionality must necessarily be the same. Also, in light of Yuan et al. which teaches that dosed individuals oral-cecal time started in some cases in less than 90 minutes, one of ordinary skill in the art would find the claims obviously claimed in the '158 patent. Although the reference application does not specifically claim oral administration, one of ordinary skill in the art would have found such administration to be obvious over Goldberg et al.

Although the instant application does not recite a method wherein the dose selected for a chronic opioid patient is at least 10% lower than the dose selected for a patient not chronically administered opioids. Nonetheless, one of ordinary skill in the art would appreciate the obviousness of treating any opioid or methadone user exhibiting the side effect of constipation with the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michel Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

19 December 2005
MG

MG

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Bruce M. Kisliuk, Director
Technology Center 1600